Amendments to the Specification

Please amend the section entitled "Description of the Drawings" on page 4 of the specification, lines 1 to 36, as follows:

Description of the Drawings

Figure 1A and B: Alignment of the VGFARP peptides with the two known VGF proteins, corresponding to the database accession No. NM_003378 and Y12661, e.g. Seq. IDs 43 and 44

Figure 2: Reverse phase chromatography for separation and enrichment of VGFARP peptides from cerebrospinal fluid

Figure 3: Mass spectrometric measurement (MALDI) on VGFARP-7 (SEQ ID NO:7) as example

Figure 4: MALDI as relatively quantifying mass spectroscopic method

Figure 5 A and B: MS/MS fragment spectrum of the peptide VGFARP-13 (SEQ ID NO:11) as example

Figure 6 [[a: - C]] A-T: Box-whisker plots for quantitative comparison of the concentrations of VGFARP-1(SEQ ID NO:1), VGFARP-2(SEQ ID NO:2), VGFARP-18(SEQ ID NO:15), VGFARP-3(SEQ ID NO:3), VGFARP-4(SEQ ID NO:4), VGFARP-5(SEQ ID NO:5), VGFARP-6(SEQ ID NO:6), VGFARP-7(SEQ ID NO:7), VGFARP-19(SEQ ID NO:16), VGFARP-20(SEQ ID NO:17), VGFARP-21(SEQ ID NO:18), VGFARP-10(SEQ ID NO:8), VGFARP-22(SEQ ID NO:19), VGFARP-28(SEQ ID NO:25), VGFARP-29(SEQ ID NO:26), VGFARP-30/32(SEQ ID NO:27 / SEQ ID NO:29), VGFARP-31(SEQ ID NO:28), VGFARP-12 (SEQ ID NO:10), VGFARP-13 (SEQ ID NO:11), VGFARP-36 (SEQ ID NO:33), and

VGFARP-37 (SEQ ID NO:34), VGFARP-40(SEQ ID NO:37), VGFARP-41 (SEQ ID NO:38) and VGFARP-42 (SEQ ID NO:39) in Alzheimer's disease patients compared with control patients.

Please amend the paragraph on page 10 of the specification, lines 11 to 26, as follows:

Peptides which can be regarded as fragments of the VGF sequence are referred to as VGFARP peptides for the purposes of this invention. They include homologous peptides derived from VGF. They include derivatives of naturally occurring alleles of these peptides and homologous mutants, especially point-mutated mutants with preferably not more than two amino acids differing from VGF. Preferred markers according to the invention are indicated in the sequence listing and thus named from VGFARP-1 (SEQ ID NO:1) to –7(SEQ ID NO:7), VGFARP-10 (SEQ ID NO:8) to –13 (SEQ ID NO:11) and VGFARP-15(SEQ ID NO:12) to -45(SEQ ID NO:42), corresponding to Seq. ID 1 to 42. The sequences of the VGFARP peptides are depicted in Figure 1A-B and in Table 1. The assignment of the VGFARP peptides to their respective Seq. ID No. is shown in Table 1.

On page 16 of the specification, please amend the paragraph beginning on line 32 and ending on line 4 of page 17 as follows:

The identification is preferably concentrated on particular peptide fragments of the VGF proteins having the GeneBank accession No. NM_003378, or the DDBJ accession No. Y12661 (Seq. IDs 43 and 44), i.e. on peptides which comprise partial sequences of these VGF proteins. These VGF peptides (VGF protein fragments) are referred to as VGF derived Alzheimer related peptide (VGFARP) and they are numbered from VGFARP-1 to VGFARP-38represented by Seq. ID 1 to 42. The connection alignment of between the VGF proteins and VGFARP peptides -1 to VGFARP-38 is depicted in Figure 1A-B. The sequences we found for the peptides are indicated in the sequence listing.

On page 35 of the specification, please amend the paragraph beginning on line 27 and ending on line 42 of page 36 as follows:

Figure 1A-B shows an alignment of the peptides of the invention with two known variants of the VGF protein which are identified in the figure by their database accession No. NM_003378 (SEQ ID NO:44) and Y12661 (SEQ ID NO:43). Sequence positions which are identical in both variants of the VGF proteins are represented by an asterisk in the sequence of NM_003378 (SEQ ID NO:44). Different sequences are represented by the amino acid code in white letters on black background. The arrow at the end or at the start of partial sequences of VGFARP-12 (SEQ ID NO:10), -13 (SEQ ID NO:11), 45 (SEQ ID NO:42) and 34 (SEQ ID NO:31) indicates that the respective sequence extends over two lines in the alignment.

On page 36 of the specification, please amend the paragraph beginning on line 24 and ending on line 33 as follows:

Figure 5A-B shows an MS/MS fragment spectrum as in Example 4 of the peptide VGFARP-13 (SEQ ID NO:11) of the invention.
Upper trace: raw data of the measurement.
Lower trace: converted, deconvoluted mass spectrum of VGFARP-13.
The peak pattern is characteristic of VGFARP-13 (SEQ ID NO:11). VGFARP-13 (SEQ ID NO:11) corresponds to the VGF sequence of Seq. ID 43 (accession No. Y12661) of amino acid 421-479.

On page 36 of the specification, please amend the paragraph beginning on line 34 and ending on line 39 as follows:

Figures 6A to 6 [[C]] T show in the form of box-whisker plots a comparison of the integrated MALDI mass spectrometric signal intensities of various VGFARP peptides in controls, compared with the signal intensities in samples from Alzheimer's disease patients.

On page 40 of the specification, please amend the paragraph beginning on line 10 and ending on line 31 as follows:

The peptides of the invention are employed in these fractions for example using nanoSpray-MS/MS [11]. This entails a VGFARP peptide ion in the mass spectrometer being selected in the mass spectrometer on the basis of its specific m/z (mass/charge) value in a manner known to the skilled worker. This selected ion is then fragmented by supplying collisional energy with an impinging gas, e.g. helium or nitrogen, and the resulting VGFARP peptide fragments are detected in the mass spectrometer in an integrated analysis unit, and corresponding m/z values are determined (principle of tandem mass spectrometry) [13]. The fragmentation behavior of peptides makes unambiguous identification of the VGFARP peptides of the invention possible when the accuracy of mass is, for example, 50 ppm by the use of computer-assisted search methods [14] in sequence databases into which the sequence of a VGF protein has been entered. In this specific case, the mass spectrometric analysis took place with a Quadrupol-TOF Instrument, QStar-Pulsar model from Applied Biosystems-Sciex, USA. Examples of MS/MS fragment spectra are shown in Figure 5A and B.

On page 40 of the specification, please amend the paragraph beginning on line 36 and ending on line 26 of page 41 as follows:

A sample preparation as in Example 1 and 2 followed by a MALDI measurement of the VGFARP peptides of the invention as in Example 3 were carried out on 222 clinical samples, i.e. 82 control samples and 130 samples from patients suffering from Alzheimer's disease. Examples of MALDI signal intensities are depicted in the form of box-whisker plots in Figures 6A to 6

[[C]] T. The box-whisker plots depicted in Figure 6 A-T are based on measurements carried out in each case on 29 to 45 samples from Alzheimer's disease patients, and 13 to 44 control samples per experiment. A total of 4 experiments was carried out. The box-whisker plots depicted make it possible to compare the integrated MALDI mass spectrometric signal intensities of various VGFARP peptides in controls with the MALDI signal intensities in samples from Alzheimer's disease patients. In these, the box, i.e. the columns in the diagrams in Figures 6A to 6 [[C]] T, in each case includes the range of MALDI signal intensities in which 50% of the respective MALDI signal intensities are to be found, and the lines starting from the box and pointing upward and downward (whiskers) indicate the range in which in each case the 25% of measurements which show the highest signal intensities (upper quarter) are to be found, and in which the 25% of measurements which show the lowest signal intensities (lower quarter) are to be found. The full line in the columns indicates the median and the broken line in the columns indicates the mean.